



US DEPARTMENT OF DEFENSE

# BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

## Preclinical Models of Blast Injury

### Hyaluronidase Administration Prior to Blast Exposure Reduced Observed Behavioral Deficits

Traumatic brain injury (TBI) resulting from exposure to Improvised Explosive Devices (IED's) may be associated with underappreciated alterations within the cerebral vasculature (*Goldstein et al. 2012*). A prominent neurological complication associated with severe TBI in casualties from Operation Iraqi Freedom and Operation Enduring Freedom from exposure to IED's was significant cerebral vasospasm (*Razumovsky et al. 2013*). Despite clinical indications of vascular insult and supporting experimental data in animals, there remains a paucity of information on specific structural and functional changes in the cerebral vascular space that occur after blast exposure. Recently, researchers at Naval Medical Research Center (Silver Spring, Maryland) have observed evidence for vascular injury in a rodent model exposed to low intensity blast overpressure (BOP).

Blast-exposed rodents demonstrated reduction of the endothelial glycocalyx structure in brain capillaries from multiple brain regions which was associated with decrements in performance in the Morris Water Maze (Figure 1). Intravenous administration of hyaluronidase (a Food and Drug Administration approved therapeutic) during the blast exposure profile was associated with a lack of observable damage to the glycocalyx and no observed behavioral decrement (*Hall et al. 2017*).

These studies elucidate the effects of exposure to BOP that are associated with mild to severe TBI outcomes on structural and functional changes in the cerebral vasculature.

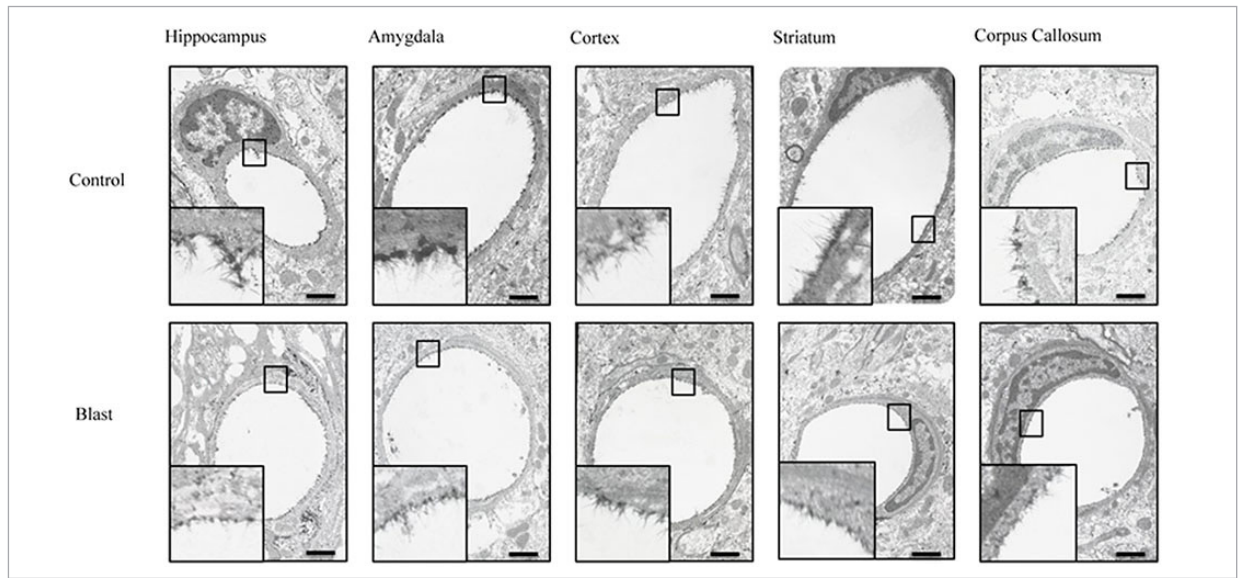
Endothelial glycocalyx degradation following repeated blast exposure is associated with behavioral decrements. Prophylactic application of hyaluronidase reduced structural abnormalities caused by repeated low-level blast exposures.

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**FIGURE 1:** Blast exposure reduced glycocalyx thickness in brain capillaries. Representative electron micrographs of capillaries from hippocampus, amygdala, cerebral cortex, corpus striatum, and corpus callosum taken from blast and sham blasted animals. Endothelial glycocalyx is the darkly stained filamentous layer present on the lumen of the capillary. All insets represent magnified image; scale bar = 500 nm. (Figure 2 from Hall et al. (2017) reproduced with permission from the authors)

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